Supplemental Data

Population Structure Can

Inflate SNP-Based

Heritability Estimates

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Table S1. Effect of Number of Principal Components on Analysis of WTCCC Data with Simulated Case-Control Phenotype

For the simulated case-control ascertainment scheme described in the main text (90% of Welsh and Scots are cases, 10% of English are cases) we compared the effect of changing the number of PCs used. We computed the mean estimated variance of phenotype explained for 100 replications of phenotype generation. A relationship cut-off of 0.05 was used in each case. The estimated values are on the liability scale, and do not adjust for incomplete LD. The difference between 0 and 5 PCs is significant, as is the difference between 5 and 10 PCs, but the difference between 10 and 20 PCs is not significant.

Number of PCs	0	5	10	20
Average estimated variance explained	40.2%	25.7%	20.4%	20.7%
Standard error	0.6%	0.7%	0.7%	0.7%

Table S2. Differences in Variance Explained with Different Relationship Cut-Off Values

For the WTCCC control data with the simulated case-control ascertainment scheme described in the main text (90% of Welsh and Scots are cases, 10% of English are cases) we compared the effect of changing the cut-off on relatedness. We computed the mean estimated variance of phenotype explained for 100 realizations of phenotype generation. The estimated values are on the liability scale, after adjustment for 20 PCs, and without adjustment for incomplete LD. The difference between a 0.05 cut-off and a 0.025 cut-off is not statistically significant. The difference between a 0.02 cut-off and a 0.05/0.025 cut-off is statistically significant. A potential explanation for this difference is that close relatives do not show as much additional phenotypic similarity as would be expected under the estimated heritability model. Thus, removing a large number of the most related people results in an increase in estimated variance explained in this case.

Relatedness cut-off	0.05	0.025	0.020
Number of individuals remaining	2861	2769	1715
Average estimated variance explained	20.7%	20.8%	30.4%
Standard error	0.7%	0.7%	1.1%